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L7 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:806608 HCAPLUS
DOCUMENT NUMBER: 133:361986
TITLE: Production of orthomyxoviruses in monkey kidney cells using protein-free media
INVENTOR(S): Kistner, Otfried; Barrett, Noel; **Mundt, Wofgang**; Dorner, Friedrich
PATENT ASSIGNEE(S): Baxter Aktiengesellschaft, Austria
SOURCE: U.S., 24 pp., Cont.-in-part of U.S. 5,753,489.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6146873	A	20001114	US 1997-849716	19971015
US 5753489	A	19980519	US 1995-487046	19950607
US 5756341	A	19980526	US 1995-483522	19950607
US 5698433	A	19971216	US 1996-684729	19960722

PRIORITY APPLN. INFO.:
US 1994-338761 B2 19941110
US 1995-483522 A2 19950607
US 1995-487046 A2 19950607
US 1995-487222 B2 19950607
US 1996-684729 A2 19960722

AB Viruses from the family Orthomyxoviridae, particularly influenza virus, can grown in monkey kidney cells, particularly Vero Cells, after passaging the cells in a serum-free or protein-free medium. The use of a proteolytic enzyme, esp. **trypsin**, also aids in the propagation of the virus. The method allows for the virus to be produced to be used in a vaccine.

IC ICM C12N007-01
ICS C12N007-08
NCL 435235100
CC 16-6 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 10, 13, 15, 63
ST Orthomyxoviridae vaccine prodn monkey kidney fermn
IT Animal cell line
(CEC (chicken embryo cell); prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)
IT Animal cell line
(CV-1; prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)
IT Animal cell line
(LLCMK2; prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)
IT Animal cell line
(MDCK; prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)
IT Animal cell line
(Vero; prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)
IT Animal tissue culture
Fermentation
Human herpesvirus 1
Influenza A virus
Influenza virus

Orthomyxoviridae
Rotavirus
Vaccines
(prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)

IT Antigens
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)

IT Antibodies
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)

IT 9002-07-7, **Trypsin** 9014-01-1, Subtilisin 9036-06-0, **Pronase**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(culture media contg.; prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)

IT 208108-78-5 307359-76-8 307359-77-9 307359-78-0 307359-79-1 307359-80-4
RL: PRP (Properties)
(unclaimed sequence; prodn. of orthomyxoviruses in monkey kidney cells using protein-free media)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:331531 HCAPLUS
DOCUMENT NUMBER: 129:26999
TITLE: Method for controlling the infectivity of viruses
INVENTOR(S): Kistner, Otfried; Barrett, Noel; **Mundt, Wolfgang**; Dorner, Friedrich
PATENT ASSIGNEE(S): Immuno A.-G., Austria
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 338,761, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5756341	A	19980526	US 1995-483522	19950607
CA 2205015	AA	19960523	CA 1995-2205015	19951110
WO 9615231	A2	19960523	WO 1995-EP4439	19951110
WO 9615231	A3	19960801		
W: CA, FI, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 791055	A1	19970827	EP 1995-937888	19951110
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, SE				
JP 10503093	T2	19980324	JP 1995-515726	19951110
JP 3158157	B2	20010423	JP 1996-515726	19951110
EP 1213030	A1	20020612	EP 2001-130212	19951110
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE				
FI 9701998	A	19970509	FI 1997-1998	19970509
US 6146873	A	20001114	US 1997-849716	19971015

PRIORITY APPLN. INFO.:

US 1994-338761	B2	19941110
US 1995-483522	A	19950607
US 1995-487046	A	19950607
US 1995-487222	A	19950607
EP 1995-937888	A3	19951110
WO 1995-EP4439	W	19951110
US 1996-684729	A2	19960722

AB A method for producing Influenza and other viruses and vaccines derived therefrom utilizes serum-free cultured vertebrate cells or vertebrate biomass aggregates to both eliminate the necessity to use costly methods requiring whole chicken embryos and, optionally, to provide proteases suitable for the activation of a wide variety of viruses. In one aspect, the method comprises the periodic or continuous removal of "treatment portions" of virus-contg. culture medium into an "augmentation loop" for treatment with a broad range of substances, such as proteases that augment the activation of the virus. Use of the loop allows utilization of such substances at high concns. while eliminating their cell toxic effects. Another aspect of the invention provides for the alteration of cleavage sites in virus proteins to thereby render them more susceptible to activation in culture. Thus, the method provides for the high yield prodn. of many viruses that can be easily scaled up to continuous large scale prodn. vols. and for resultant vaccines which are free of egg proteins and are much more economical to produce.

IC ICM C12N007-02
ICS A61K039-145
NCL 435235100
CC 15-2 (Immunochemistry)

ST virus antigen cell culture protease vaccine; influenza hemagglutinin serum free culture vaccine

IT Animal cell line
(CV-1; virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT Animal cell line
(LLCMK2; virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT Animal cell line
(Vero; virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT Culture media
(serum-free; virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT Mutagenesis
(site-directed; virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT Enzymes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(subtilisin-like; virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT Egg
(**trypsin** inhibitor; virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT Animal cell line
Animal virus
Biomass
Blood serum
Carriers
Containers
Influenza virus
Kidney

Mammal (Mammalia)
Monkey
Vaccines
(virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT Antigens
Hemagglutinins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT 208108-78-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(virus antigen vaccine produced by serum free cell culture and treatment with protease)

IT 8049-47-6, Pancreatin 9001-75-6, Pepsin 9001-92-7, Protease 9002-07-7, **Trypsin** 9004-06-2, Elastase 9004-07-3, **Chymotrypsin** 9014-01-1, Subtilisin 9031-98-5, Carboxypeptidase 9035-81-8, **Trypsin** inhibitor 9036-06-0, **Pronase** 9073-78-3, Thermolysin 9087-70-1, Aprotinin 37259-58-8, Serine protease 141760-45-4, Furin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(virus antigen vaccine produced by serum free cell culture and treatment with protease)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:435985 HCAPLUS
DOCUMENT NUMBER: 127:47061
TITLE: Protein preparation by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes
INVENTOR(S): Fischer, Bernhard; **Mitterer, Artur**; Dorner, Friedrich; Eibl, Johann
PATENT ASSIGNEE(S): Immuno Aktiengesellschaft, Austria
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 776969	A2	19970604	EP 1996-890172	19961119
EP 776969	A3	19990602		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, IT, LI, NL, SE				
AT 9501927	A	19980515	AT 1995-1927	19951124
AT 404597	B	19981228		
CA 2190802	AA	19970525	CA 1996-2190802	19961120
US 6010844	A	20000104	US 1996-752892	19961120
NO 9604965	A	19970526	NO 1996-4965	19961122
JP 09183794	A2	19970715	JP 1996-330278	19961125

PRIORITY APPLN. INFO.: AT 1995-1927 19951124

AB Proteins and esp. enzymes prepd. by controlled proteolysis of pro-proteins are disclosed. Pro-protein is put in soln. with proteinase and in the presence of a carrier that has a higher affinity for protein than for

pro-protein. Then the protein is be selectively adsorbed onto the carrier. Recombinant prothrombin (factor II) activation to thrombin (IIa) by immobilized **trypsin** is in several examples. Thrombin is then purified using affinity chromatog.

IC ICM C12N009-00
ICS C12P021-06; C12N009-10; C12N009-64; C07K014-755; C07K014-815

CC 7-2 (Enzymes)
Section cross-reference(s): 3, 9

ST protein pro controlled proteolysis recombinant; enzyme pro controlled proteolysis recombinant; proenzyme controlled proteolysis protease; proprotein controlled proteolysis proteinase

IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); NUU (Other use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(immobilized, carrier; protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

IT Blood-coagulation factors
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(pro-; protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(proproteins; protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

IT Affinity chromatography
Immobilization, biochemical
(protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

IT Zymogens
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

IT Enzymes, preparation
Proteins, general, preparation
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

IT 618-39-3D, Benzamidine, immobilized 8001-27-2D, Hirudin, immobilized 9005-49-6D, Heparin, immobilized, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); NUU (Other use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(carrier; protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

IT 9001-26-7P, Prothrombin
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

IT 9002-04-4P, Thrombin
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL

(Biological study); PREP (Preparation)
(protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)
IT 9001-92-7, Proteinase 9001-92-7D, Proteinase, immobilized 9002-07-7, **Trypsin** 9002-07-7D, **Trypsin**, immobilized
RL: CAT (Catalyst use); NUU (Other use, unclassified); USES (Uses)
(protein prepn. by controlled proteolysis of pro-proteins including recombinant pro-proteins and pro-enzymes)

L7 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:574900 HCAPLUS
DOCUMENT NUMBER: 125:215380
TITLE: Immobilized hirudin and hirudin-based peptides used for the purification of recombinant human thrombin prepared from recombinant human prothrombin
AUTHOR(S): Fischer, Bernhard E.; **Mitterer, Artur**; Schlokat, Uwe; Grillberger, Leopold; **Reiter, Manfred**; **Mundt, Wolfgang**; Dorner, Friedrich; Eibl, Johann
CORPORATE SOURCE: Biomedical Res. Center, Immuno AG, Orth a.d. Donau, A-2304, Austria
SOURCE: Protein Expression and Purification (1996), 8(2), 167-174
CODEN: PEXPEJ; ISSN: 1046-5928
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A simple and efficient activation-affinity purifn. system was developed to obtain thrombin from recombinant CHO cells expressing human prothrombin. In this method, a controllable process for the activation of recombinant prothrombin is directly coupled with a purifn. strategy for the recombinant thrombin generated. At a const. flow rate and with a contact time limited to few seconds, recombinant prothrombin was filtered through immobilized **trypsin**. In a closed flow system, the recombinant thrombin generated was filtered through newly designed thrombin-specific affinity gels. Hirudin, the most specific thrombin inhibitor, and hirudin-based peptides were covalently immobilized to Sepharose, thus creating thrombin-specific affinity gels that immediately absorb the thrombin generated from the activation mixt. Prothrombin and incompletely activated mols. did not bind to the affinity gel and were recirculated for a further activation cycle. Due to the specificity of the affinity gels for thrombin and the elimination of thrombin from the activation mixt., proteolytic degrdn. and autocatalytic inactivation of the recombinant thrombin was prevented. Recombinant thrombin was isolated from the hirudin-based affinity gels by chaotrope salt elution, resulting in high yields of highly pure, active thrombin. Affinity purifn. of thrombin was not deleteriously affected by contamination of the starting material with other proteins. Activation and affinity purifn. were equally effective for recombinant and human plasma-derived prothrombin as well as for human and recombinant thrombin.
CC 7-2 (Enzymes)
ST thrombin prothrombin purifn property hirudin
IT 9001-26-7P, Prothrombin 9002-04-4P, Thrombin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(immobilized hirudin and hirudin-based peptides used for the purifn. of recombinant human thrombin prepd. from recombinant human prothrombin)
IT 8001-27-2, Hirudin
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical

process); PROC (Process); USES (Uses)
(immobilized hirudin and hirudin-based peptides used for the purifn. of recombinant human thrombin prepd. from recombinant human prothrombin)

L7 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:440965 HCAPLUS
DOCUMENT NUMBER: 125:84835
TITLE: Method for producing biologicals in protein-free culture
INVENTOR(S): Kistner, Otfried; Barrett, Noel; **Mundt, Wolfgang**; Dorner, Friedrich
PATENT ASSIGNEE(S): Immuno Aktiengesellschaft, Austria
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615231	A2	19960523	WO 1995-EP4439	19951110
WO 9615231	A3	19960801		
W: CA, FI, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5753489	A	19980519	US 1995-487046	19950607
US 5756341	A	19980526	US 1995-483522	19950607
EP 791055	A1	19970827	EP 1995-937888	19951110
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, SE				
JP 10503093	T2	19980324	JP 1995-515726	19951110
FI 9701998	A	19970509	FI 1997-1998	19970509

PRIORITY APPLN. INFO.:
US 1994-338761 A 19941110
US 1995-483522 A 19950607
US 1995-487046 A 19950607
US 1995-487222 A 19950607
WO 1995-EP4439 W 19951110

AB The present invention includes an approach for producing viruses, such as influenza, and vaccines derived therefrom as well as recombinant proteins derived from viral vectors, by utilizing vertebrate cells cultured under protein-free conditions. These cells, which include a cellular biomass, show improved capabilities for propagating viruses and eliminate the need for costly and time-consuming viral passaging and purifn. The invention also includes further approaches for enhancing the propagation of viruses by employing activating substances, modifying the activation site of viruses, and using augmentation loops. Improved approaches for producing viral reassortants also are provided.

IC ICM C12N007-00
ICS C12P021-00; C12N005-00; A61K039-145; C07K014-11; A61K039-15; A61K039-245

CC 16-6 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 63

ST virus culture vertebrate cell vaccine prodn

IT Vaccines
Virus, animal
(producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Animal tissue culture
(vertebrate; producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Animal cell line

(CV-1, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(Epstein-Barr, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(Junin, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Animal cell line
(LLCMK2, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(Lassa, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Animal cell line
(MDBK, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Animal cell line
(MDCK, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Animal cell line
(MRC-5, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Animal cell line
(Vero, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Animal cell line
(WI-38, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(adeno-, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(cytomegalo-, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(hepatitis A, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(hepatitis C, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(herpes simplex 1, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(herpes simplex 2, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(influenza, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(measles, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(mumps, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal
(polio-, producing viruses and vaccines in protein-free culture in vertebrate cells)
IT Virus, animal

(reovirus 3, producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Virus, animal
(respiratory syncytial, producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Virus, animal
(rota-, producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Virus, animal
(rubella, producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Virus, animal
(tick-borne encephalitis, producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Virus, animal
(vaccinia, producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Virus, animal
(varicella-zoster, producing viruses and vaccines in protein-free culture in vertebrate cells)

IT Virus, animal
(yellow fever, producing viruses and vaccines in protein-free culture in vertebrate cells)

IT 9001-92-7, Protease 9014-01-1, Subtilisin 9035-81-8, **Trypsin** inhibitor 9036-06-0, **Pronase** 9073-78-3, Thermolysin 9087-70-1, Aprotinin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in prodn. of viruses and vaccines in protein-free culture in vertebrate cells)